

# MEETING ABSTRACT

# Open Access

# Inhaled nitric oxide: an sGC-dependent IOP lowering agent

Wolfgang S Lieb<sup>1</sup>, Stefan Munster<sup>1</sup>, Ana C Dordea<sup>1</sup>, Sara Vandenwijngaert<sup>1</sup>, Robert E Tainsh<sup>1</sup>, Peter Brouckaert<sup>2</sup>, Warren M Zapol<sup>1</sup>, Emmanuel S Buys<sup>1\*</sup>

From 7th International Conference on cGMP Generators, Effectors and Therapeutic Implications  
Trier, Germany. 19-21 June 2015

## Background

The nitric oxide (NO)-soluble guanylate cyclase (sGC)-cyclic guanosine 3'5'-monophosphate (cGMP) pathway regulates intraocular pressure (IOP). Preclinical and clinical studies have demonstrated the ability of NO-donor compounds to lower IOP (e.g. VESNEO<sup>®</sup>). The use of inhaled NO gas (iNO), a specific pulmonary but not systemic vasodilator, is an approved therapy for pulmonary hypertension and is under development as a treatment for other cardiovascular diseases (e.g. for myocardial ischemia, the NOMI trial). We hypothesized that breathing NO lowers IOP in an sGC-dependent manner.

## Methods

**Anesthetized IOP model:** 10- to 20-week-old male wild-type (WT) mice and mice deficient in the  $\alpha 1$ -subunit of sGC (sGC $\alpha 1^{-/-}$  mice; n=9, each) were anesthetized with isoflurane using a standard protocol resulting in a stable IOP baseline. Ten minutes after baseline measurement, IOP was measured again in mice breathing 1.8 % isoflurane and either control gas (N<sub>2</sub> balanced in O<sub>2</sub>) or 40 ppm

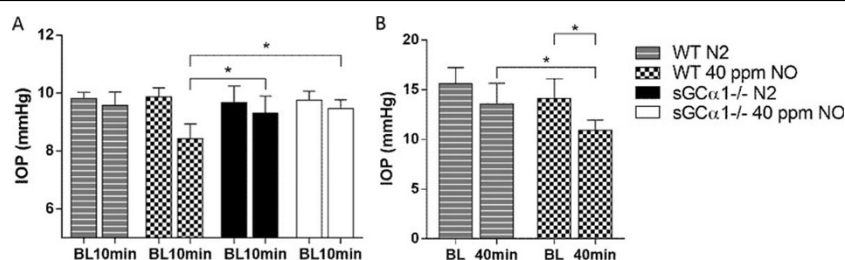
NO balanced in O<sub>2</sub>. **Awake IOP model:** WT mice were acclimated to awake IOP measurements (every other day for 2 weeks). 40 min after baseline measurements, IOP was measured in mice breathing either control gas or 40 ppm iNO (n=8, each) in an incubation chamber.

## Results

Breathing control gas did not affect IOP in WT or sGC $\alpha 1^{-/-}$  mice (Figure 1). Breathing iNO decreased IOP in both anesthetized WT mice (9.86±0.31 vs. 8.42±0.51 mmHg at baseline and after iNO, respectively, Figure 1a) and awake WT mice (14.13±1.95 vs. 10.93±1.01 mmHg, at baseline and after 40 min iNO, respectively, Figure 1b). In contrast, iNO did not lower IOP in sGC $\alpha 1^{-/-}$  mice (9.75±0.31 vs. 9.46±0.30 mmHg at baseline and after iNO, respectively, Figure 1a).

## Conclusion

Inhalation of 40 ppm iNO decreased IOP in anesthetized and awake WT mice but not in sGC $\alpha 1^{-/-}$  mice. These findings confirm that NO is an IOP-lowering



**Figure 1** iNO decreases IOP in WT but not sGC $\alpha 1^{-/-}$  mice:

\* Correspondence: ebuys@mgh.harvard.edu

<sup>1</sup>Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, 02114, MA, USA  
Full list of author information is available at the end of the article

agent, and identify NO-gas as a possible therapeutic approach to acutely lower IOP. In addition, our results identify sGC as the downstream target of NO's ability to lower IOP. sGC stimulators, under development for treatment of cardiovascular diseases, such as the recently approved ADEMPAS<sup>®</sup>, may be considered as a novel treatment option for elevated IOP.

#### Authors' details

<sup>1</sup>Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, 02114, MA, USA.

<sup>2</sup>Department for Biomedical Molecular Biology, Ghent University, Ghent, 9000, Belgium.

Published: 2 September 2015

doi:10.1186/2050-6511-16-S1-A38

**Cite this article as:** Lieb et al.: Inhaled nitric oxide: an sGC-dependent IOP lowering agent. *BMC Pharmacology and Toxicology* 2015 **16**(Suppl 1):A38.

**Submit your next manuscript to BioMed Central  
and take full advantage of:**

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
[www.biomedcentral.com/submit](http://www.biomedcentral.com/submit)

